Remarks

Upon entry of the foregoing amendment, claims 1, 3, 4, 6, 8-13, 15-20, 22 and 23 are pending in the application. Claims 2, 5, 7, 14 and 21 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. New claims 22 and 23 are sought to be added. The new claims are supported by, for example, original claims 7 and 21. Claims 3, 4, 6, 8-13 and 15-20 have been amended to put the claims into conformance with domestic practice. The abstract has been amended to put it into conformance with 37 C.F.R. § 1.72(b). These changes are believed to introduce no new matter, and their entry is respectfully requested.

It is believed that the application is now in condition for examination. Early notice to this effect is respectfully requested.

Respectfully submitted,

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Version with markings to show changes made

Abstract:

The present invention relates generally to the modulation of arteriogenesis and/or the growth of collateral arteries or other arteries from preexisting arteriolar connections. In particular, the present invention provides a method for enhancing arteriogenesis and/or the growth of collateral arteries and/or other arteries from preexisting arteriolar connections comprising contacting an organ, tissue or cells with transforming growth factor beta 1 (TGFβ1) or a nucleic acid molecule encoding TGFβ1. The present invention also relates to [the use of TGFβ1 or a nucleic acid molecule encoding TGFβ1 for the preparation of pharmaceutical compositions for enhancing arteriogenesis and/or collateral growth of collateral arteries and/or other arteries from preexisting arteriolar connections. Furthermore, the present invention relates to] a method for the treatment of tumors comprising contacting an organ, tissue or cells with an agent which suppresses arteriogenesis and/or the growth of collateral arteries and/or other arteries from preexisting arteriolar connections through the inhibition of the biological activity of TGFβ1. [The present invention further involves the use of an agent which suppresses arteriogenesis and/or the growth of collateral arteries and/or other arteries from preexisting arteriolar connections through the inhibition of the biological activity of TGFβ1 for the preparation of pharmaceutical compositions for the treatment of tumors.]

Claims:

3. (once amended) The method of claim 1 [or the use of claim 2], wherein the TGFβ1 is a recombinant TGFβ1.

4. (once amended) The method of claim [claims] 1 [or 3], further comprising contacting the organ, tissue or cells [cell] with a growth factor or cytokine.

6. (once amended) The method of claim 4 [or the use of claim 5], wherein said growth factor or cytokine is b-FGF, PDGF, TNF-α, IL-1, IL-6 or VEGF.

8. (once amended) The method of [any one of claims] claim 1[, 3, 4, 6 or 7 or the use of any one of claims 2, 3, 5 or 6], wherein the TGFβ1 is a derivative or [functional] functionally equivalent substance.

9. (once amended) The method [or use] of claim 8, wherein said derivative or [functional] functionally equivalent substance is an antibody, (poly)peptide, nucleic acid, small organic compound, ligand, hormone, PNA or peptidomimetic.

10. (once amended) The method of [any one of claims] claim 1[, 3, 4, 6 to 9 or the use of any one of claims 2, 3, 5, 6, 8 or 9], wherein said method [or said pharmaceutical composition] is [designed to be] applied to a subject suffering from a vascular disease or a cardiac infarct or a stroke.

11. (once amended) The method [or the use] of claim 10, wherein said vascular disease is arteriosclerosis and/or a hyperlipidemic condition, a coronary artery disease, cerebral occlusive disease, peripheral occlusive disease, visceral occlusive disease, renal artery disease, mesenterial arterial insufficiency or an ophthalmic [ophtamic] or retinal [retenal] occlusion.

12. (once amended) The method of [any one of claims] claim 1[, 3, 4, 6 to 11 or the use of any one of claims 2, 3, 5, 6, 8 to 11], wherein said method [or said pharmaceutical composition] is [designed to be] applied to a subject during or after exposure to an agent or radiation or surgical treatment which damage or destroy arteries.

13. (once amended) A method for the treatment of tumors comprising contacting an [organs] organ, tissue or cells with an agent which suppresses arteriogenesis and/or the growth of collateral arteries and/or other arteries from preexisting arteriolar connections through inhibition of the biological activity of TGFβ1 [as defined in any one of claims 1 to 12].

15. (once amended) The method of claim 13 [or the use of claim 14], wherein the agent inhibits the biological activity of TGFβ1 and/or inhibits an intracellular signal or signal cascade comprising SMAD proteins triggered in macrophages through the receptor for TGFβ1.

16. (once amended) The method [or the use] of claim 15, wherein the agent blocks an interaction of the TGFβ1 and its receptor.

17. (once amended) The method of [any one of claims] claim 13[, 15 or 16 or the use of any one of claims 14 to 16], wherein the agent is derived from a class of substances [as defined in claim 9] selected from the group consisting of: an antibody, (poly)peptide, nucleic acid, small organic compound, ligand, hormone, PNA and peptidomimetic.

18. (once amended) The method [or the use] of claim 17, wherein the agent is [designed to be] expressed in vascular cells or cells surrounding preexisting arteriolar connections to a tumor.

19. (once amended) The method of [any one of claims] claim 13 [or 15 to 18 or the use of any one of claims 14 to 18], wherein the tumor is a vascular tumor.

20. (once amended) The method [or the use] of claim 19, wherein the tumor is selected form the group consisting of: Colon Carcinoma, Sarcoma, Carcinoma in the breast, Carcinoma in the head/neck, Mesothelioma, Glioblastoma, Lymphoma and Meningeoma.